

EP04/09781

PCT/EP200 4 / 0 0 9 7 8 1



Europäisches
Patentamt

European
Patent Office

Office européen
des brevets

25. 10. 2004

Bescheinigung

Certificate

Attestation

REC'D 09 DEC 2004

WIPO

PCT

Die angehefteten Unterla-
gen stimmen mit der
ursprünglich eingereichten
Fassung der auf dem näch-
sten Blatt bezeichneten
europäischen Patentanmel-
dung überein.

The attached documents
are exact copies of the
European patent application
described on the following
page, as originally filed.

Les documents fixés à
cette attestation sont
conformes à la version
initialement déposée de
la demande de brevet
européen spécifiée à la
page suivante.

Patentanmeldung Nr. Patent application No. Demande de brevet n°

03019881.6

**PRIORITY
DOCUMENT**
SUBMITTED OR TRANSMITTED IN
COMPLIANCE WITH RULE 17.1(a) OR (b)

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
p.o.

R C van Dijk

BEST AVAILABLE COPY



Europäisches
Patentamt

European
Patent Office

Office européen
des brevets

Anmeldung Nr:

Application no.: 03019881.6

Demande no:

Anmeldetag:

Date of filing: 02.09.03

Date de dépôt:

Anmelder/Applicant(s)/Demandeur(s):

Roche Vitamins AG
Grenzacherstrasse 124
4070 Basel
SUISSE

Bezeichnung der Erfindung/Title of the invention/Titre de l'invention:

(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.

If no title is shown please refer to the description.

Si aucun titre n'est indiqué se referer à la description.)

Method of stabilizing ascorbyl phosphate and salts thereof

In Anspruch genommene Priorität(en) / Priority(ies) claimed / Priorité(s)
revendiquée(s)

Staat/Tag/Aktenzeichen/State/Date/File no./Pays/Date/Numéro de dépôt:

Internationale Patentklassifikation/International Patent Classification/
Classification internationale des brevets:

A23K/

Am Anmeldetag benannte Vertragstaaten/Contracting states designated at date of
filing/Etats contractants désignées lors du dépôt:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL
PT RO SE SI SK TR LI

BEST AVAILABLE COPY

Roche Vitamins AG, CH-4070 Basle, Switzerland

Case 21914

BEST AVAILABLE COPY

5

Method of stabilizing ascorbyl phosphate and salts thereof

The present invention relates to a method of stabilizing ascorbyl phosphates against degradation by phosphatases. Ascorbyl phosphates are used in feedstuff industry as an additive to feed for pets and other animals. Such feed may contain active phosphatases which may lead to degradation of ascorbyl phosphates. It has now been found that ascorbyl phosphates can be stabilized against degradation by phosphatases by coating with lipids. Thus, the present invention relates to a method of stabilizing ascorbyl phosphates against degradation by phosphatases by coating with lipids. The invention further relates to novel compositions comprising certain lipid-coated ascorbyl phosphates as well as animal feed and feed premixes containing them.

Vitamin C preparations which are coated with lipids to stabilize vitamin C against the impact of external influences such as atmosphere, moisture, light and heat are known from EP 0 443 743. These known preparations mandatorily contain vitamin E in the coating. By the present invention, it has surprisingly been found that ascorbyl phosphates can be stabilized against phosphatases by lipid coating in the absence of vitamin E. Indicating that primary stressor for phosphorylated vitamin C is not oxidation.

The term "ascorbyl phosphate" as used herein denotes metal salts of phosphoric acid esters of ascorbic acid wherein at least one hydroxy group of the ascorbic acid molecule is

- 2 -

BEST AVAILABLE COPY

esterified with phosphoric acid. Typical ascorbyl phosphates for use in the present invention are trisodium L-ascorbyl-2-phosphate and sodium calcium L-ascorbyl-2-phosphate which are commercially available as STAY-C50 and ROVIMIX STAY-C35, respectively (Roche Vitamins AG, Basel). The amount of ascorbyl phosphate or salt thereof in the stabilized compositions is such to provide between about 5wt.-% to about 40 wt.-%, based on ascorbic acid equivalents.

The term "lipid" as used herein comprises mono-, di- and triglycerides of fatty acids, fatty acid sucrose and propyleneglycol esters and the like, and waxes, phospholipids and sugar lipids, as well as mixtures of the foregoing. Particular examples of lipids are soybean oil, palm oil, rapeseed oil, coconut oil, and the like. Preferred are hydrogenated plant oils and glycerol stearates. The amount of lipid is about 10 wt.-% to about 60 wt.-%, based on the total weight of the composition.

- 15 The coated ascorbyl phosphate compositions may further contain adsorbants, e.g., polysaccharides such as starch and modified starch, or calcium silicate alone or a mixture of calcium silicate with one of the following mixture components: microcrystalline cellulose, magnesium silicate, magnesium oxide, stearic acid, calcium stearate, magnesium stearate, hydrophilic silicic acid, dicalcium phosphate, tricalcium phosphate and kaolin.
- 20 The amount of adsorbant, if present, is about 0.5 wt.-% to about 5 wt.-%, based on the total weight of the composition.

The coated ascorbyl phosphate compositions can be manufactured by dispersing the ascorbyl phosphate in the liquified (by heating) lipid and subsequent processing the melt into a solid composition, e.g., a granulate by procedures known per se, e.g. by spraying the melt in cold air, or by coating the ascorbyl phosphate with liquid lipid in a fluidized bed.

The so obtained granulate is, suitably, collected in or coated by an adsorbant, e.g., such as disclosed above. The so-obtained granulate is stabilized against degradation by phosphatases: When 10 mg of granulate containing 15% of ascorbic acid activity were exposed during 60 minutes to 30 mg of acid phosphatase (Roche Diagnostics GmbH, Mannheim, Germany) diluted in 20 ml of water, more than 80 % of the ascorbyl phosphate remained unchanged. Moreover, the granulate is free-flowing, non-dusting and non-caking.

Granulate compositions as disclosed above, wherein the ascorbyl phosphate is trisodium L-ascorbyl-2-phosphate, or sodium calcium-2-ascorbyl phosphate, and mixtures thereof, are novel and, as such, also are an object of the present invention.

- 5 The coated ascorbyl phosphate composition is conventionally mixed into a premix containing in addition vitamin, minerals and other additives. The premix is added to feed, mixed, stored and then subjected to a hydrothermal treatment, e.g. pelleting, extrusion or retorting to produce diets for animals such as pets and fish. The diets typically contain components of animal origin, such as fish, fish parts, fish meal, fats, meat, meat
- 10 byproducts. Accordingly, it is important that the incorporated composition protects the ascorbic acid activity from extended exposure to phosphatases present in these components.

The following Examples illustrate the invention further.

15

Example 1

- 300 g of hardened palm oil having a melting point of 46°C were heated to 75 °C. 400 g of ROVIMIX STAY-C 35, which contain 140 g ascorbic acid activity, were added to a
- 20 fluidized air bed granulator. The oil was then added to the fluidized bed and the resulting powder collected.

There was obtained a beige, granulated powder with a content of 20% ascorbic acid activity. When 10 g of the product was exposed to humid air of 75% rH, weight increased was 0.27 g and the product remained free-flowing.

25

Example 2

- 112 g of glycerol monostearate having a melting point of 60°C were heated to 90 °C. 888 g of STAY-C 50, which contain 400 g ascorbic activity, were added to a fluidized air bed granulator. The oil was then added to the fluidized bed and the resulting powder collected.
- 30 10 g of hydrophobic silicic acid were then added. The resulting powder contained 40 % ascorbic acid activity. The product passed through an Agway flow tunnel having an opening of 11 mm.

Example 3

- 35 1346 g of of castor oil having a melting point of 65°C were heated to 90 °C. 1000 g of ROVIMIX STAY-C 35, which contained 350 g ascorbic activity, were slowly added to the vessel and dispersed in the oil. The mixture was then sprayed in a fluidized bed flushed

BEST AVAILABLE COPY

- 4 -

with cool air of 5°C. The resulting powder was collected. The resulting powder was free-
flowing and contained 15% ascorbic acid activity.

BEST AVAILABLE COPY

What is claimed is:

1. A method of stabilizing an ascorbyl phosphate against degradation by phosphatases
5 which comprises coating said ascorbyl phosphate with a lipid.
2. A method as in claim 1 wherein the ascorbyl phosphate salt is trisodium ascorbyl-2-phosphate, or sodium calcium ascorbyl-2-phosphate.
- 10 3. A method as in claim 1 or 2 wherein the lipid is a wax or plant oil.
4. A method as in any of claims 1 - 3 wherein an adsorbant is additionally present .
5. A method as in any one of claims 1-4 the amount of ascorbyl phosphate is such to
15 provide between about wt.5 % to about 40 wt.-% ascorbic acid equivalents.
6. A method as in any one of claims 1-5 wherein the amount of lipid is about 10 wt.-% to about 60 wt.-%, based on the total weight of the composition.
- 20 7. A method as in any one of claims 1-6 wherein an adsorbant is present in an amount of about 0.5 wt.-% to about 5 wt.-%, based on the total weight of the composition.
8. A method as in any one of claims 1-7 wherein a granulate having an average mean particle size of about 0.1 to about 1.0 mm is prepared.
25
9. Granulate compositions comprising trisodium L-ascorbyl-2-phosphate or sodium calcium-2-ascorbyl phosphate or mixtures thereof, and a lipid.
10. Granulate compositions as in claim 9 wherein the lipid is a wax or plant oil.
— 30 —
11. Granulate compositions as in claim 9 or 10 wherein the amount of trisodium L-ascorbyl-2-phosphate or sodium calcium-2-ascorbyl phosphate in the granulate is such to provide between about 5 -% to about 40 wt.-%, ascorbic acid equivalents.
- 35 12. Granulate compositions as in any one of claims 9-11 wherein the amount of lipid is about 10 wt.-% to about 60 wt.-%, based on the total weight of the composition.

- 6 -

13. Granulate compositions as in any one of claims 9-12 wherein the amount of adsorbant, if present, is about 0.5 wt.-% to about 5 wt.-%, based on the total weight of the composition.

5

14. Granulate compositions as in any one of claims 9-13 wherein the granulate has a mean particle size of about 0.1 to about 1.0 mm.

10

15. Animal feed and feed premixes containing a granulate composition as claimed in any one of claims 9-14.

15

20

BEST AVAILABLE COPY

Fax Cover Sheet

Roche**Vitamins**

To: Europäisches Patentamt,
München Tel. +49 89 23 99-0
Fax +49 89 23 99 44 65

Copies:

From: Dr. L. Grossner Roche Vitamins Ltd
Patent Department
CH-4070 Basel
Tel. +41-61-687 09 56
Fax +41-61-688 32 41

Date: September 2, 2003

No. of pages: 13 (incl. cover sheet)

BEST AVAILABLE COPY